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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,206	10/17/2001	Samuel Achilefu	MRD- 74	5790

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EXAMINER
JONES, DAMERON L

ART UNIT	PAPER NUMBER
1616	11

DATE MAILED: 07/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/981,206	Applicant(s) -	
	Examin r D. L. Jones	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/17/01; 6/9/03; and 6/26/03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-7 and 20-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,9 and 15-19* is/are rejected.

7)☒ Claim(s) *10-14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *10* .
5) ☐ Notice of Informal Patent Application (PTO-152) .
6) ☐ Other:

CLARIFICATION OF THE RECORD

1. In order to allow Applicant a broader search of the invention, a restriction as set forth below was performed.

APPLICANT'S INVENTION

2. Applicant's invention is directed to compounds and methods thereof comprising Formula 3 as set forth in independent claims 1 and 8.

Note: Claims 1-22 are pending.

RESTRICTION INTO GROUPS

3. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-7, drawn to compounds having Formula 3 as set forth in independent claim 1, classified in class 548, subclass 100+.

II. Claims 8-19, drawn to a method of performing a diagnostic procedure as set forth in independent claim 8, classified in class 424, subclass 9.6.

III. Claims 8-15, drawn to a method of performing a therapeutic procedure as set forth in independent claim 8, classified in class 514, subclass 359.

Note: Claims appearing in more than one group will only be examined to the extent that they read on the elected invention.

4. The inventions are distinct, each from the other because of the following reasons:

Inventions (I and II) and (I and III) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product as claimed may be used in a diagnostic or therapeutic procedure.

5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

ELECTION OF SPECIES

6. This application contains claims directed to the following patentably distinct species of the claimed invention: the various compounds (and uses thereof) having Formula 3 wherein the variables W1 and W2 may be the same or different and are selected from the group consisting of CR10R11, O, NR12, S, and Se. The species classify differently depending upon the variable values assigned to W1 and W2; thus, generating distinct species.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

7. During a telephone conversation with Ms. Beverly Lyman on 6/26/03 a provisional election was made with traverse to prosecute the invention of Group II (the group directed to a method of performing a diagnostic procedure as set forth in independent claim II, claims 8-19. Likewise Applicant elected to prosecute the species set forth in Paper No. 9, filed 6/9/03. The species of Formula 3 wherein W1 and W2 are

CR10R11, Y1, Y2, Z1, and Z2 are (CH2)a-CONH-Bm; X1 and X2 are nitrogen; Q is oxygen; K1 and K2 are CH2; R1 through R9 are hydrogen; R10 and R11 are C(CH3)2; A1 is a single bond; and A1, B1, C1, and D1 form a six-membered carbocyclic ring. Affirmation of this election must be made by applicant in replying to this Office action. ***Note***: (Please see the attached interviews summary detailing the 'new' restriction).

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

WITHDRAWN CLAIMS

9. Claims 1-7 and 20-22 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

103 REJECTION(S)

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 8, 9, and 15-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Licha et al (US Patent No. 6,083,485).

Licha et al disclose in vivo diagnoses using a dye in the near infrared radiation region. The method uses water-soluble dyes and their biomolecule adducts as contrast agents for fluorescence and transillumination diagnostics (see entire document, especially, abstract). The conjugates comprise a biological detecting unit (B), a dye showing a maximum absorption in the range of 650 to 1200 nanometers (F), and a hydrophilic group that improves water solubility (W). The biological detecting unit may be an amino acid, a peptide, a complementarity determining region, an antigen, a hapten, an enzyme substrate, an enzyme cofactor, biotin, a carotinoid, a hormone, a neurohormone, a neurotransmitter, a growth factor, a lymphokin, a lectin, a toxin, a carbohydrate, an oligosaccharide, a polysaccharide, a dextrane, an oligonucleotide, or a receptor bonding pharmaceutical (column 4, lines 35-63). The in vivo diagnostic method involves administering one or several conjugates comprising B-F-W and irradiating the conjugate with light from the visible to the near infrared range of 650 to 1200 nanometers and generating an image from the data obtained (column 8, lines 42-49). The method may be used for the visualization of tissue without pathological alterations, systemic diseases, tumors, blood vessels, atherosclerotic plaques, and perfusion and diffusion (column 9, lines 30-34). Various dyes, in particular, a dye of Formula V, may be used for in vivo diagnosis (columns 10-11, bridging paragraph). While the instant invention does not specify the other components that may be present

in their method, Licha et al disclose dyes that are encompassed in Applicant's Formula 3.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Achilefu et al using the teachings of Licha et al and generate a method of performing a diagnostic method as set forth in independent claim 8. In particular, Licha et al disclose that their conjugate comprises a biological detecting unit, a dye, and a hydrophilic group that improves water-solubility and that their invention may be used for in vivo diagnosis when administered to tissues. Thus, the instant invention and Licha et al differ in that the instant invention does not state the other components that may be present for use in the diagnostic method. Instead, the instant invention is directed to a method of performing a diagnostic procedure comprising administering a cyanine dye bioconjugate. Furthermore, a dye of Formula V may be used (columns 10-11, bridging paragraph). The dye is encompassed in the instant invention when Q is the fragment as set forth in column 11, line 25; X and Y are independently O or S; and R28 and R29 are hydrogen.

12. Claims 8, 9, and 15-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Turner et al (US Patent No. 6,329,531).

Turner et al disclose optical diagnostic agents for diagnosis of neurodegenerative diseases. The compounds of Turner et al may be used for in vivo diagnosis using a dye in the near infrared radiation region. The method uses contrast agents for fluorescence and transillumination diagnosis (see entire document,

especially, abstract). The conjugates comprise a dye signal molecule which has at least one absorption maximum in the range of 600 to 1200 nanometers (F), a biomolecule that binds to beta-amyloid plaques (A), a dye (B), and a hydrophilic low molecular structural element that binds to beta amyloid plaques (W) [column 2, lines 41-57]. The dye may have Formula II (column 3, lines 46-54). The variable A may be an antibody, antibody fragment, specific peptide and proteins, receptors, enzymes, enzymes substrates, nucleotides, ribonucleic acids, deoxyribonucleic acids, lipoproteins, carbohydrates, mono-, di-, or trisaccharides, oligo- or polysaccharides, or dextran (column 6, lines 20-26). The in vivo diagnostic method involves administering one or several conjugates comprising F-A-B-W and irradiating the conjugate with light from the near infrared region and generating an image from the data obtained (column 9, lines 6-20). Various dyes, in particular, a dye of Formula II, may be used for in vivo diagnosis (column 3, lines 46-54). While the instant invention does not specify the other components that may be present in their method, Licha et al disclose dyes that are encompassed in Applicant's Formula 3.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Achilefu et al using the teachings of Turner et al and generate a method of performing a diagnostic method as set forth in independent claim 8. In particular, Turner et al disclose that their conjugate comprises components F-A-B-W and may used for in vivo diagnosis of amyloid plaques. Thus, the instant invention and Turner et al differ in that the instant invention does not state the other components that may be present for use in the diagnostic method. Instead, the

instant invention is directed to a method of performing a diagnostic procedure comprising administering a cyanine dye bioconjugate. Furthermore, a dye of Formula 3 may be used (column 3, lines 46-54). The dye is encompassed in the instant invention when Q is the fragment as set forth in column 4, line 40 (see the second fragment); X is independently O or S; E1 = hydrogen; R5 and R6 = E1 radical; R11 = hydrogen, fluorine, chlorine, bromine, iodine, nitro group, or oE1 wherein E 1 = alkyl; and R28 and R29 are hydrogen.

CLAIM OBJECTIONS

13. Claims 10-13 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Note: Claims 10-13 are allowable over the prior art of record because the prior art neither anticipates nor renders obvious the additional limitations present in the dependent claims in combination with those of independent claim 8 and its intervening claims.

COMMENTS/NOTES

14. It should be noted that the full scope of Group II has been examined.

15. Did Applicant intend to write 'Y1' instead of 'Y2' on the left half of the structure having the 5-membered ring? Please make the appropriate corrections.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (703) 308-4640. The examiner can normally be reached on Mon.-Fri. (alternate Mon.), 6:45 a.m. - 4:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (703) 308 - 2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

D. L. Jones
Primary Examiner
Art Unit 1616

July 2, 2003